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#6	Search Epstein-Barr virus and lupus and cross- antigen Limits: Entrez Date to 1996/01/13	08:42:36	8
#5	Search Epstein-Barr virus and lupus Limits: Entrez Date to 1996/01/13	08:42:19	138
#4	Search Harley J and Epstein-Barr virus Limits: Entrez Date to 1996/01/13	08:42:00	1
#3	Search Harley J and lupus Limits: Entrez Date to 1996/01/13	08:40:55	51
#2	Search Harley J and EBV Limits: Entrez Date to 1996/01/13	08:40:47	0
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L4 60 BINDING AND L3

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(TARGETING OR TARGETINGS)
L5 3 TARGETING AND L4

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L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:991150 CAPLUS
DOCUMENT NUMBER: 140:35913
TITLE: Breast homing peptides binding to
aminopeptidase P in breast vasculature
identified by phage display and use thereof as
targeting drugs for breast cancer treatment
INVENTOR(S): Ruoslahti, Erkki; Essler, Markus
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 30 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003232762	A1	20031218	US 2002-158566	20020529
PRIORITY APPLN. INFO.:			US 2002-158566	20020529

AB The present invention provides a method of directing a moiety to breast vasculature in a subject by administering to the subject a conjugate which contains a moiety linked to a homing mol. that selectively homes to breast vasculature, whereby the moiety is directed to breast vasculature. In one embodiment, the homing mol. is a peptide containing the amino acid sequence PGPEGAG, or a peptidomimetic thereof. The above peptide is derived from a cyclic nonapeptide, CPGPEGAGC, isolated from a T7 phage CX7C library, where C is cysteine and X is any amino acid. This cyclic peptide CPGPEGAGC homes to normal breast tissue with a 100-fold selectivity over nontargeted phage. Specifically, it binds to the vascular endothelium in the breast but not in other tissues, and binds to the vasculature of hyperplastic and malignant lesions in transgenic breast cancer mice. Furthermore, the aminopeptidase P is identified as the receptor for cyclic CPGPEGAGC breast homing and the binding of aminopeptidase P to insolubilized CPGPEGAGC can be blocked by its free cognate synthetic peptide, or apstatin (a synthetic inhibitor of aminopeptidase P), or an anti-aminopeptidase P antibody. In contrast, the anti-aminopeptidase P antibody does not block the breast homing of another peptide CRSS, which might bind distinct target receptors in breast tissue. This breast homing peptides may be useful in designing drugs for the prevention and treatment of breast cancer.

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:185320 CAPLUS
DOCUMENT NUMBER: 136:242932
TITLE: Identification of peptide ligands for specific cell
types by phage display for use in drug
targeting and control of biological processes
INVENTOR(S): Arap, Wadih; Pasqualini, Renata

PATENT ASSIGNEE(S) : Board of Regents, the University of Texas System, USA
 SOURCE: PCT Int. Appl., 311 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020769	A1	20020314	WO 2001-US27692	20010907
WO 2002020769	A9	20030904		
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EP 1322755	A1	20030702	EP 2001-968603	20010907
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WO 2003022991	A2	20030320	WO 2002-US27836	20020830
WO 2003022991	A3	20041028		
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EP 1497314	A2	20050119	EP 2002-757531	20020830
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WO 2004020999	A1	20040311	WO 2002-US34987	20021030
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AU 2002364501	A1	20040319	AU 2002-364501	20021030
EP 1546714	A1	20050629	EP 2002-799873	20021030
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US 2004170955	A1	20040902	US 2003-363204	20031006
US 2005003466	A1	20050106	US 2004-784537	20040223
US 2006094672	A1	20060504	US 2004-489071	20041013
US 2006239968	A1	20061026	US 2006-530168	20060223

PRIORITY APPLN. INFO.:	US 2000-231266P	P 20000908
	US 2001-765101	A 20010117
	WO 2001-US27692	W 20010907
	WO 2002-US27836	W 20020830
	WO 2002-US34987	W 20021030

AB The present invention concerns methods and compns. for in vivo and in vitro targeting. A large number of targeting peptides directed towards human organs, tissues or cell types are disclosed. The peptides are of use for targeted delivery of therapeutic agents, including but not limited to gene therapy vectors. A novel class of gene therapy vectors is disclosed. Certain of the disclosed peptides have therapeutic use for inhibiting angiogenesis, inhibiting tumor growth, inducing apoptosis, inhibiting pregnancy or inducing weight loss. Methods of identifying novel targeting peptides in humans, as well as identifying endogenous receptor-ligand pairs are disclosed. Methods of identifying novel infectious agents that are causal for human disease states are also disclosed. A novel mechanism for inducing apoptosis is further disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2002:185294 CAPLUS
 DOCUMENT NUMBER: 136:227943
 TITLE: Chimeric molecules for targeting proteins to the Skp1-Cullin-F box complex for ubiquitination and degradation
 INVENTOR(S): Deshaies, Raymond J.; Crews, Craig; Sakamoto, Kathleen M.
 PATENT ASSIGNEE(S): California Institute of Technology, USA; Yale University; The Regents of the University of California
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020740	A2	20020314	WO 2001-US42158	20010910
WO 2002020740	A3	20020808		
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AU 2001095041	A5	20020322	AU 2001-95041	20010910
EP 1322750	A2	20030702	EP 2001-975749	20010910
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US 2004038358	A1	20040226	US 2002-299203	20021118
PRIORITY APPLN. INFO.:			US 2000-231359P	P 20000908
			US 2001-953473	A2 20010910
			WO 2001-US42158	W 20010910

AB The present invention is based on the discovery that an ubiquitin pathway protein ubiquitinates any target protein once the ubiquitin pathway protein and the target protein are placed in proximity by a chimeric construct that binds the ubiquitin pathway protein and the target protein.

Accordingly the present invention provides a composition that ubiquitinates a target protein. The composition comprises an ubiquitin pathway protein binding moiety and a targeting moiety, wherein the ubiquitin pathway protein binding moiety recognizes an ubiquitin pathway protein and the targeting moiety recognizes a target protein and wherein the ubiquitin pathway protein binding moiety is coupled to the targeting moiety. In addition, the present invention provides libraries of compns., where each composition contains an ubiquitin pathway protein binding moiety and a member of a mol. library, which can be used to identify proteins involved in a predetd. function of cells. The intracellular levels of many proteins are regulated by ubiquitin-dependent proteolysis. One of the best-characterized enzymes that catalyzes the attachment of ubiquitin to proteins is a ubiquitin ligase complex, Skp1-Cullin-F box complex containing Hrt1 (SCF). We sought to artificially target a protein to the SCF complex for ubiquitination and degradation. To this end, we tested methionine aminopeptidase-2 (MetAP-2), which covalently binds the angiogenesis inhibitor ovalicin. A chimeric compound, protein-targeting chimeric mol. 1 (Protac-1), was synthesized to recruit MetAP-2 to SCF. One domain of Protac-1 contains the I_KB_α phosphopeptide that is recognized by the F-box protein β-TRCP, whereas the other domain is composed of ovalicin. We show that MetAP-2 can be tethered to SCFβ-TRCP, ubiquitinated, and degraded in a Protac-1-dependent manner. In the future, this approach may be useful for conditional inactivation of proteins, and for targeting disease-causing proteins for destruction.

=> L4 and therapeutic
 222894 THERAPEUTIC
 22911 THERAPEUTICS
 239884 THERAPEUTIC
 (THERAPEUTIC OR THERAPEUTICS)
 L6 5 L4 AND THERAPEUTIC

=> D L6 IBIB ABS 1-5

L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:71066 CAPLUS
 DOCUMENT NUMBER: 142:170050
 TITLE: DEF domain-containing members of the MAP kinase pathway and their use in screening for drug inhibitors
 INVENTOR(S): Blenis, John; Murphy, Leon O.
 PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
 SOURCE: PCT Int. Appl., 104 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007090	A2	20050127	WO 2004-US21514	20040702
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SN, TD, TG
 PRIORITY APPLN. INFO.: US 2003-484761P P 20030703
 AB Mitogen-activated protein (MAP) kinases (e.g., ERK1/2) phosphorylate a variety of target proteins including, for example, several immediate-early gene products (e.g., Fos, Myc, and Jun family proteins). Certain phosphorylation reactions require binding of the MAP kinase to the DEF domain of the target protein. Inhibitors that block this interaction may be useful therapeutics for human disease, including as antineoplastic agents. This invention provides several advantages over known therapies that directly target the MAP kinase signaling cascade. Typically, most compds. that inhibit the MAP kinase pathway are non-specific and inhibit more than one enzyme, and the targeted inhibited kinases are not available to perform normal physiol. functions necessary for cell survival, whereas therapeutic methods of the present invention inhibit the activation of particular target proteins and leave the MAP kinases enzymically active and available to phosphorylate other non-DEF domain-containing proteins. Thus, DEF domains are identified in a large number of proteins, and the principles of the invention are exemplified using the immediate-early gene, c-Fos. Screening assays useful for identifying compds. that inhibit the MAP kinase-DEF domain interaction are also disclosed.

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2002:185320 CAPLUS
 DOCUMENT NUMBER: 136:242932
 TITLE: Identification of peptide ligands for specific cell types by phage display for use in drug targeting and control of biological processes
 INVENTOR(S): Arap, Wadih; Pasqualini, Renata
 PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
 SOURCE: PCT Int. Appl., 311 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020769	A1	20020314	WO 2001-US27692	20010907
WO 2002020769	A9	20030904		
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AU 2001088843	A5	20020322	AU 2001-88843	20010907
EP 1322755	A1	20030702	EP 2001-968603	20010907
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US 2005003466	A1 20050106	US 2004-784537	20040223
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		US 2001-765101	A 20010117
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		WO 2002-US34987	W 20021030

AB The present invention concerns methods and compns. for in vivo and in vitro targeting. A large number of targeting peptides directed towards human organs, tissues or cell types are disclosed. The peptides are of use for targeted delivery of therapeutic agents, including but not limited to gene therapy vectors. A novel class of gene therapy vectors is disclosed. Certain of the disclosed peptides have therapeutic use for inhibiting angiogenesis, inhibiting tumor growth, inducing apoptosis, inhibiting pregnancy or inducing weight loss. Methods of identifying novel targeting peptides in humans, as well as identifying endogenous receptor-ligand pairs are disclosed. Methods of identifying novel infectious agents that are causal for human disease states are also disclosed. A novel mechanism for inducing apoptosis is further disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:164204 CAPLUS
 DOCUMENT NUMBER: 128:184573
 TITLE: Intestinal Peptide and Protein Delivery: Novel Bioadhesive Drug-Carrier Matrix Shielding from Enzymic Attack
 AUTHOR(S): Bernkop-Schnuerch, Andreas; Pasta, Martina
 CORPORATE SOURCE: Center of Pharmacy Institute of Pharmaceutical Technology, University of Vienna, Vienna, A-1090, Austria
 SOURCE: Journal of Pharmaceutical Sciences (1998), 87(4), 430-434
 CODEN: JPMSAE; ISSN: 0022-3549
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal

LANGUAGE: English
AB We have been developing a novel bioadhesive drug-carrier matrix that protects embedded therapeutic peptides and proteins from degradation by the most abundant intestinal proteases. Increasing amts. of the Bowman-Birk inhibitor (BBI) were thereby covalently linked to chitosan-EDTA. The bioadhesive properties of the resulting polymer-BBI conjugates and their inhibitory effect toward trypsin (EC 3.4.21.4), chymotrypsin (EC 3.4.21.1), elastase (3.4.21.36), carboxypeptidase A (EC 3.4.17.1), and aminopeptidase N (EC 3.4.11.2) were evaluated in vitro. Whereas unmodified chitosan-EDTA exhibited under our exptl. conditions an adhesive strength of 54.4 ± 7.7 mN, it was determined to be 21.0 ± 3.8 mN for the comparably most adhesive polymer-BBI conjugate (mean \pm SD; n = 5). All polymer-BBI conjugates showed a strong inhibitory activity toward the serine proteases trypsin and chymotrypsin. However, the protective effect toward elastase was markedly lower. Due to the high binding affinity of chitosan-EDTA toward zinc, which represents an essential cofactor for carboxypeptidase A and aminopeptidase N, all polymer-BBI conjugates displayed addnl. a strong protective effect toward these exopeptidases. The novel bioadhesive polymer-BBI conjugates described in this study seem to be very useful drug-carrier matrixes in overcoming the enzymic barrier to orally administered peptide and protein drugs.

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:154462 CAPLUS
DOCUMENT NUMBER: 128:248433
TITLE: Synthesis and in vitro evaluation of chitosan-EDTA-protease-inhibitor conjugates which might be useful in oral delivery of peptides and proteins
AUTHOR(S): Bernkop-Schnurch, Andreas; Scerbe-Saiko, Andreas
CORPORATE SOURCE: Center of Pharmacy, Institute of Pharmaceutical Technology, University of Vienna, Vienna, A-1090, Austria
SOURCE: Pharmaceutical Research (1998), 15(2), 263-269
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel mucoadhesive polymer that protects peptide drugs from degradation by secreted as well as membrane-bound proteases in the intestine was developed and this polymer was evaluated in vitro. The serine protease inhibitors antipain, chymostatin and elastatinal were covalently linked to chitosan (poly-[1 \rightarrow 4]- β -D-glucosamine). Thereafter, the complexing agent EDTA was bound to the remaining primary amino groups of the polymer. The inhibitory effect of the resulting polymer-conjugate towards trypsin (EC 3.4.21.4), chymotrypsin (EC 3.4.21.1), elastase (3.4.21.36), carboxypeptidase A (EC 3.4.17.1), carboxypeptidase B (EC 3.4.17.2) and aminopeptidase N (EC 3.4.11.2) as well as its mucoadhesive properties were evaluated in vitro. Whereas the novel polymer-conjugate exhibited excellent swelling properties, its adhesive force was under our assay conditions 42% lower than that of unmodified chitosan. However, the polymer-conjugate showed a strong inhibitory activity towards all tested serine proteases. Due to its addnl. high binding affinity towards bivalent metal ions, it also inhibited the Zn²⁺-dependent exopeptidases carboxypeptidase A, B and aminopeptidase N. The novel mucoadhesive polymer-conjugate described in this study seems to be a useful tool in overcoming the enzymic barrier to perorally administered therapeutic peptides and proteins.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:102217 CAPLUS
 DOCUMENT NUMBER: 116:102217
 TITLE: Molecular recognition units
 INVENTOR(S): Rodwell, John D.; McKearn, Thomas J.; Alvarez, Vernon
 L.; Radcliffe, Robert D.
 PATENT ASSIGNEE(S): Cytogen Corp., USA
 SOURCE: PCT Int. Appl., 71 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9117173	A1	19911114	WO 1991-US3116	19910507
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5196510	A	19930323	US 1990-519702	19900507
EP 527954	A1	19930224	EP 1991-911988	19910507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
PRIORITY APPLN. INFO.:			US 1990-519702	A 19900507
			US 1988-291730	B2 19881229
			WO 1991-US3116	W 19910507

AB A novel mol. recognition unit (MRU) (protein or polypeptide containing a binding site of or for a ligand) is identified and/or designed and prepared by (1) stimulating production of B-lymphocytes specific for an antigen or a hapten containing a mol. recognition site complementary to the site to be mimicked; (2) immortalizing the B-cells; (3) identifying B-cells which secrete IgM binding to the antigen or hapten; (4) further screening for early B-cells in which the deoxyribonucleotide sequence expressed is rearranged in only 1 complementarity-determining region (CDR) compared to that of germline genes; (5) determining the nucleotide sequence in this region or the corresponding amino acid sequence; and (6) synthesizing the MRU encoded by the nucleotide sequence. The MRU optimally comprises <40-45 amino acid residues. The MRU may be conjugated or fused with an effector domain, optionally via a linker moiety, for diagnostic or therapeutic use. Suitable ligands include antigens, hormones, pheromones, neurotransmitters, signal proteins and peptides, prostaglandins, etc. Thus, thrombus-binding fusion peptides were prepared chemical in which the MRU constituted CDR3 of monoclonal antibody PAC-1 (Taub, et al., 1989) engineered to have enhanced affinity for activated platelet fibrinogen receptor, and the effector domain quant. bound metal ions. A 99mTc-labeled fusion peptide was injected i.v. into rabbits for imaging of blood clots with a gamma camera. Background clearance of the peptide was rapid owing to its low mol. weight, and the peptide was not immunogenic.

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